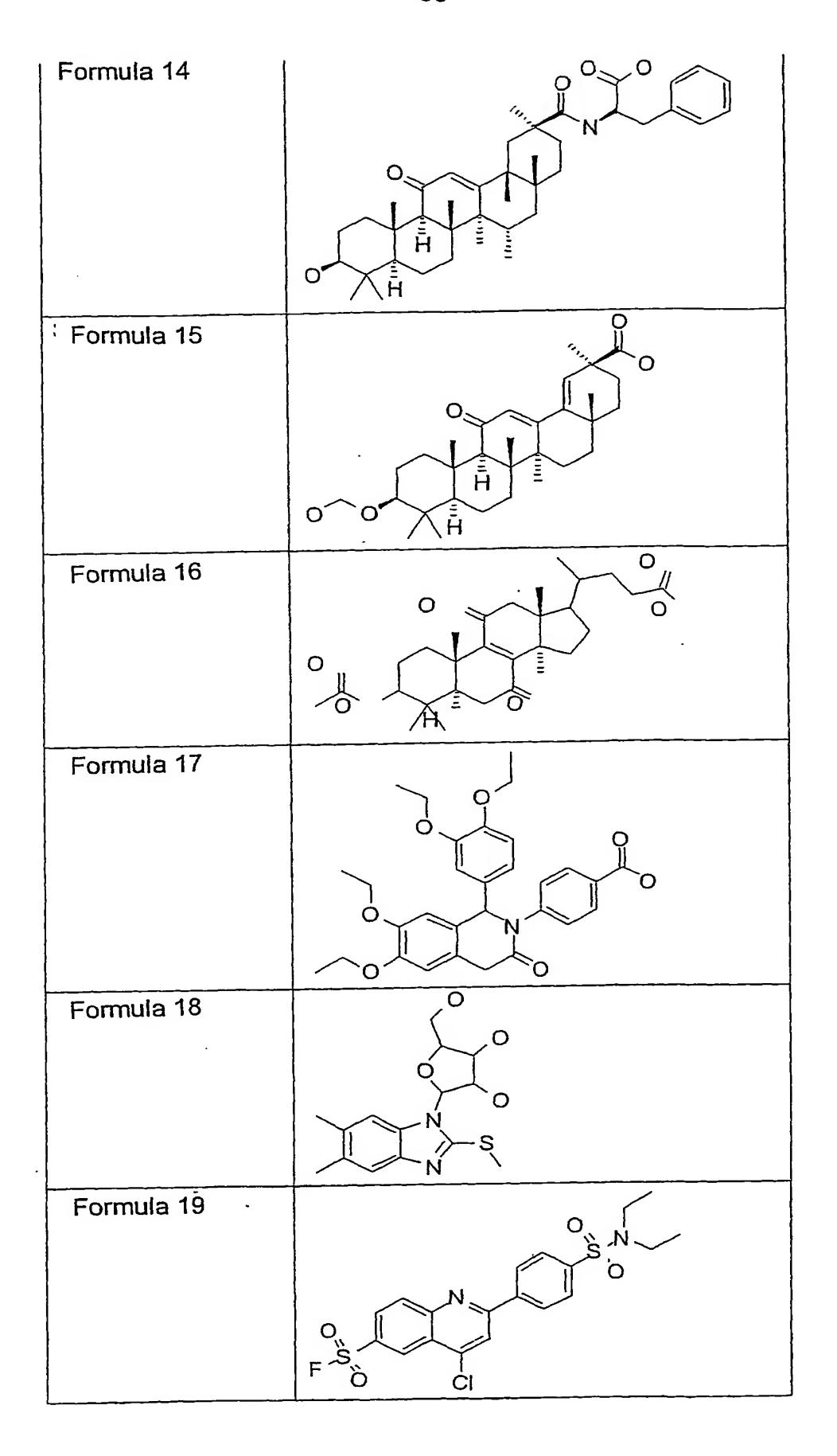
Claims

- Use of an 11-β-HSD-type 1 and/or type 2 inhibitor or a pharmaceutically acceptable salt thereof, for the manufacture of a pharmaceutical agent for the prevention and/or treatment of inflammation-induced and/or immune-mediated loss of bone and/or cartilage.
- 2. The use according to claim 1 for the prevention and/or treatment of inflammation-induced and/or immune-mediated loss of bone and/or cartilage in a mammal.
- 3. The use according to claim 2, wherein the mammal is a human.
- 4. The use according to any one of claims 1 to 3, wherein said use is for the prevention and/or treatment of osteoporosis, postmenopausal osteoporosis, Paget's disease, lytic bone metastases, arthritis, juvenile chronic arthritis and/or adjuvant arthritis, infectious diseases, bone loss by cancer, bone loss by HIV, tooth loss, bone marrow inflammation, synovial inflammation, cartilage and/or bone erosion and/or proteoglycan damage.
- 5. The use according to claim 4, wherein said use is for the prevention and/or treatment of periodontitis and/or arthritis selected from the group consisting of osteoarthritis and/or rheumatoid arthritis.
- 6. The use according to any one of claims 1 to 5, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor is selected from the group consisting of the following formulas:

Compound	Structure
Name	
Formula 1	
Formula 2	Br O O N N N N N N N N N N N N N N N N N
Formula 3	
Formula 4	
Formula 5	N.N.O.O.O.
Formula 6	
Formula 7	

Formula 8	N PO
	SNOO
Formula 9	CI CI
Formula 10	ONSON-N-N-SCI
Formula 11	N S O CI
Formula 12	
Formula 13	



Formula 20	
·	
Formula 21	N O O O O O O O O O O O O O O O O O O O
Formula 22	
Formula 23	
Formula 24	
Formula 25	

Formula 26	
Formula 27	
Formula 28	N N N O
Formula 29	
Formula 30	S N N O N N O O
Formula 31	Br Cl

The use according to any one of claims 1-5, wherein the 11-β-HSD-7. type 1 and/or type 2 inhibitor has the structure of formula I:

formula l

wherein R1 is

a hydrogen,

a linear or branched C₁-C₁₀ alkyl group,

a linear or branched C₁-C₁₀ alkenyl group,

a linear or branched C₁-C₁₀ alkynyl group,

an ester, amino, halo, hydroxy, carbonyl, carboxy, carboxyphenoxy, C₁-C₄ alkoxy, C₁-C₄ alkoxy carbonyl, C₁-C₄ alkyl amino, di-(C₁-C₄-alkyl) amino, cyano, carboxy amide, carboxy-(C1-C4-alkyl)amino, carboxy-di (C₁-C₄-alkyl)sulfo, sulfido (C₁-C₄-alkyl), sulfoxido (C₁-C₄-alkyl), sulfono (C₁-C₄-aminoalkyl) or thio group, a saturated or unsaturated, aromatic or heteroaromatic mono- or polycyclic group,

wherein said cyclic group may be mono- or polysubstituted with an ester, amino, halo, hydroxy, C₁-C₄ alkoxy, carboxy, carbonyl, C₁-C₄ alkoxycarbonyl, carboxyphenoxy, C₁-C₄ alkyl amino, di-(C₁-C₄-alkyl) amino, cyano, carboxy amide, carboxy-(C1-C4-alkyl)amino, carboxy-di (C₁-C₄-alkyl)amino, sulfo, sulfido (C₁-C₄-alkyl), sulfoxido (C₁-C₄-alkyl), sulfono (C1-C4-alkyl), thio, C1-C4 alkyl, C2-C4 alkenyl or C2-C4 alkynyl group;

R² is

hydrogen, C1-C4 alkyl, carbonyl, ester, amino, halo, carbonyl,

hydroxy, carboxy, carboxyphenoxy, C_1 - C_4 alkoxy, C_1 - C_4 alkoxy carbonyl, C_1 - C_4 alkyl amino, di- $(C_1$ - C_4 -alkyl)amino, cyano, carboxy amide, carboxy- $(C_1$ - C_4 -alkyl)amino, carboxy-di(C_1 - C_4 -alkyl), sulfo, sulfido (C_1 - C_4 -alkyl), sulfoxido (C_1 - C_4 -alkyl), sulfono (C_1 - C_4 -alkyl) or thio group;

R³ is

a hydrogen,

a linear or branched C₁-C₁₀ alkyl group,

a linear or branched C₁-C₁₀ alkenyl group,

a linear or branched C₁-C₁₀ alkynyl group,

an ester, amino, halo, hydroxy, carbonyl, carboxy, carboxyphenoxy, C_1 - C_4 alkoxy, C_1 - C_4 alkoxy carbonyl, C_1 - C_4 alkyl amino, di- $(C_1$ - C_4 -alkyl) amino, cyano, carboxy amide, carboxy- $(C_1$ - C_4 -alkyl)amino, carboxy-di $(C_1$ - C_4 -alkyl)sulfo, sulfido $(C_1$ - C_4 -alkyl), sulfoxido $(C_1$ - C_4 -alkyl) or thio group, a saturated or unsaturated, aromatic or heteroaromatic mono- or polycyclic group;

wherein the chemical bond from carbon 13 to 14 is saturated or unsaturated;

or a salt or derivative thereof in the form of an individual enantiomer, diastereomer or a mixture thereof.

8. The use according to claim 7, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor is selected from the group consisting of the following formulas:

9. The use according to any one of claims 1-5, wherein the $11-\beta$ -HSD-type 1 and/or type 2 inhibitor has the structure of formula II:

wherein R1 is

- a hydrogen,
- a linear or branched C₁-C₁₀ alkyl group,
- a linear or branched C₁-C₁₀ alkenyl group,
- a linear or branched C₁-C₁₀ alkynyl group,

an ester, amino, halo, hydroxy, carbonyl, carboxy, carboxyphenoxy, C_1 - C_4 alkoxy, C_1 - C_4 alkoxy carbonyl, C_1 - C_4 alkyl amino, di- $(C_1$ - C_4 -alkyl) amino, cyano, carboxy amide, carboxy- $(C_1$ - C_4 -alkyl)amino, carboxy-di $(C_1$ - C_4 -alkyl)sulfo, sulfido $(C_1$ - C_4 -alkyl), sulfoxido $(C_1$ - C_4 -alkyl), sulfoxido $(C_1$ - C_4 -aminoalkyl), thio group, a saturated or unsaturated, aromatic or heteroaromatic mono- or polycyclic group,

wherein said cyclic group may be mono- or polysubstituted with an ester, amino, halo, hydroxy, C_1 - C_4 alkoxy, carbonyl, carboxy, C_1 - C_4 alkoxycarbonyl, carboxyphenoxy, C_1 - C_4 alkyl amino, di- $(C_1$ - C_4 -alkyl) amino, cyano, carboxy amide, carboxy- $(C_1$ - C_4 -alkyl)amino, carboxy-di $(C_1$ - C_4 -alkyl)amino, sulfo, sulfido $(C_1$ - C_4 -alkyl), sulfoxido $(C_1$ - C_4 -alkyl), thio, C_1 - C_4 alkyl, C_2 - C_4 alkenyl or C_2 - C_4 alkynyl group;

R² is a hydrogen or C₁-C₄ alkyl,

R³ and R⁴ are each selected from

- a hydrogen
- a linear or branched C₁-C₁₀ alkyl group,
- a linear or branched C₁-C₁₀ alkenyl group,
- a linear or branched C₁-C₁₀ alkynyl group,

an ester, amino, halo, hydroxy, carbonyl, carboxy, carboxyphenoxy, C_1 - C_4 alkoxy, C_1 - C_4 alkoxy carbonyl, C_1 - C_4 alkyl amino, di- $(C_1$ - C_4 -alkyl) amino, cyano, carboxy amide, carboxy- $(C_1$ - C_4 -alkyl)amino, carboxy-di $(C_1$ - C_4 -alkyl)sulfo, sulfido $(C_1$ - C_4 -alkyl), sulfoxido $(C_1$ - C_4 -alkyl), sulfono $(C_1$ - C_4 -aminoalkyl), thio group, a saturated or unsaturated, aromatic or heteroaromatic mono- or polycyclic group;

 R^5 is a hydrogen, C_1 - C_4 alky, carbonyl, ester, amino, halo, hydroxy, carboxy, carboxyphenoxy, C_1 - C_4 alkoxy, C_1 - C_4 alkoxy carbonyl, C_1 - C_4 alkyl amino, di-(C_1 - C_4 -alkyl)amino, cyano, carboxy amide, carboxy-(C_1 - C_4 -alkyl)amino, carboxy-di(C_1 - C_4 -alkyl), sulfo, sulfo, sulfido (C_1 - C_4 -alkyl), sulfoxido (C_1 - C_4 -alkyl), sulfono (C_1 - C_4 -alkyl) or thio group,

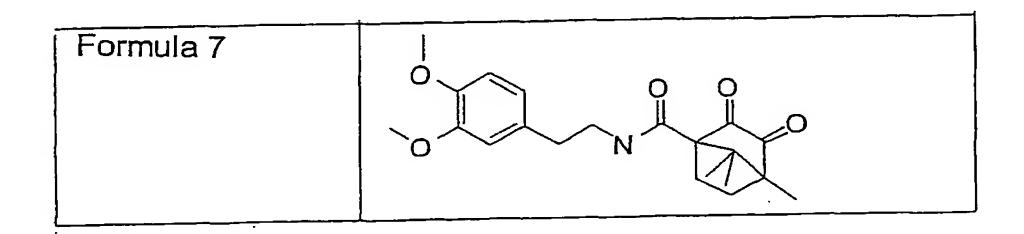
wherein the chemical bond from carbon 8 to 9 is saturated or unsaturated;

wherein the chemical bond from carbon 13 to 14 is saturated or unsaturated;

or a salt or derivative thereof in the form of an individual enantiomer, diastereomer or a mixture thereof.

10. The use according to claim 9, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor is:

11. The use according to claim 6, wherein the 11-β-HSD-type 1 and/or type2 inhibitor is:

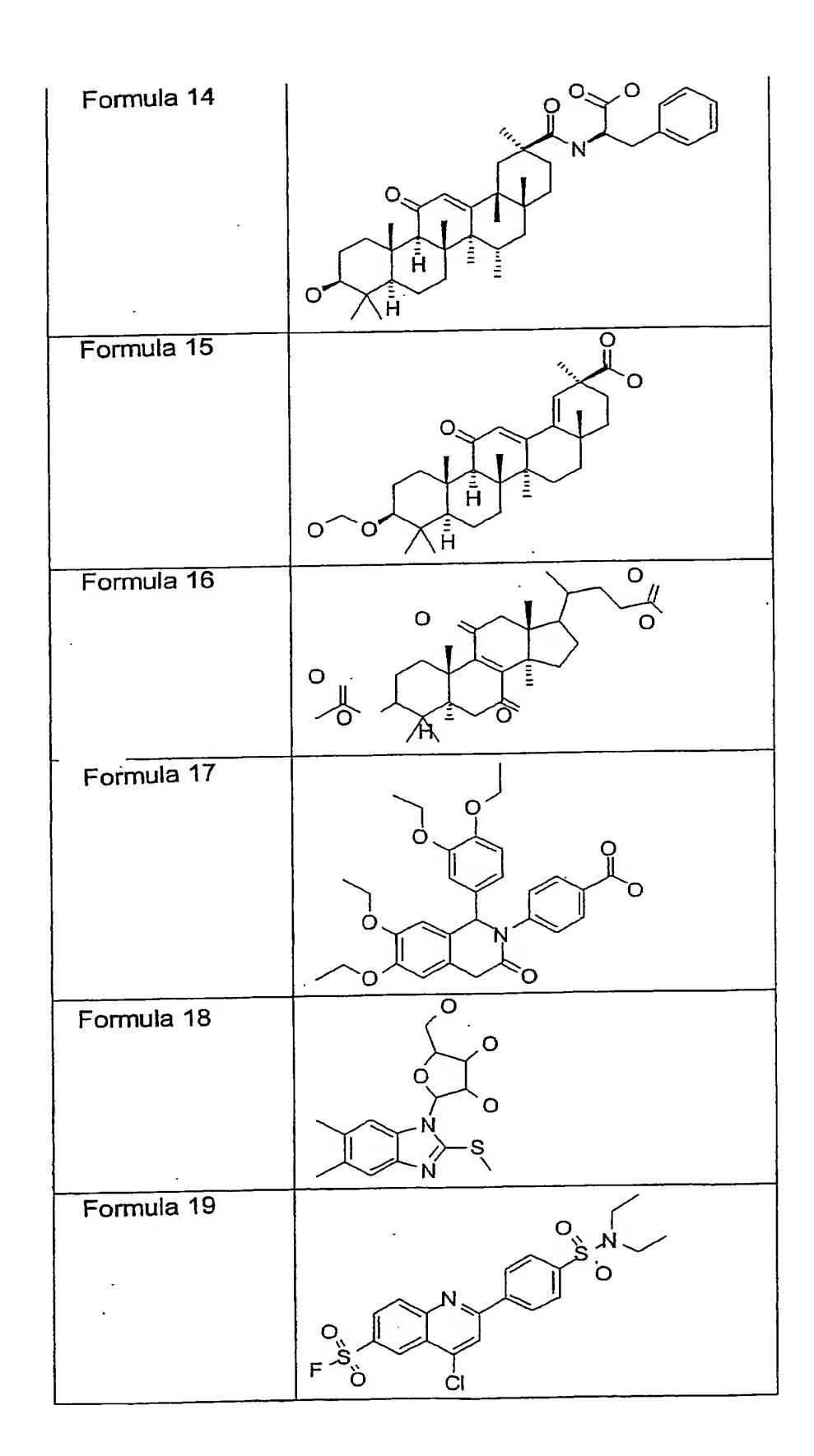


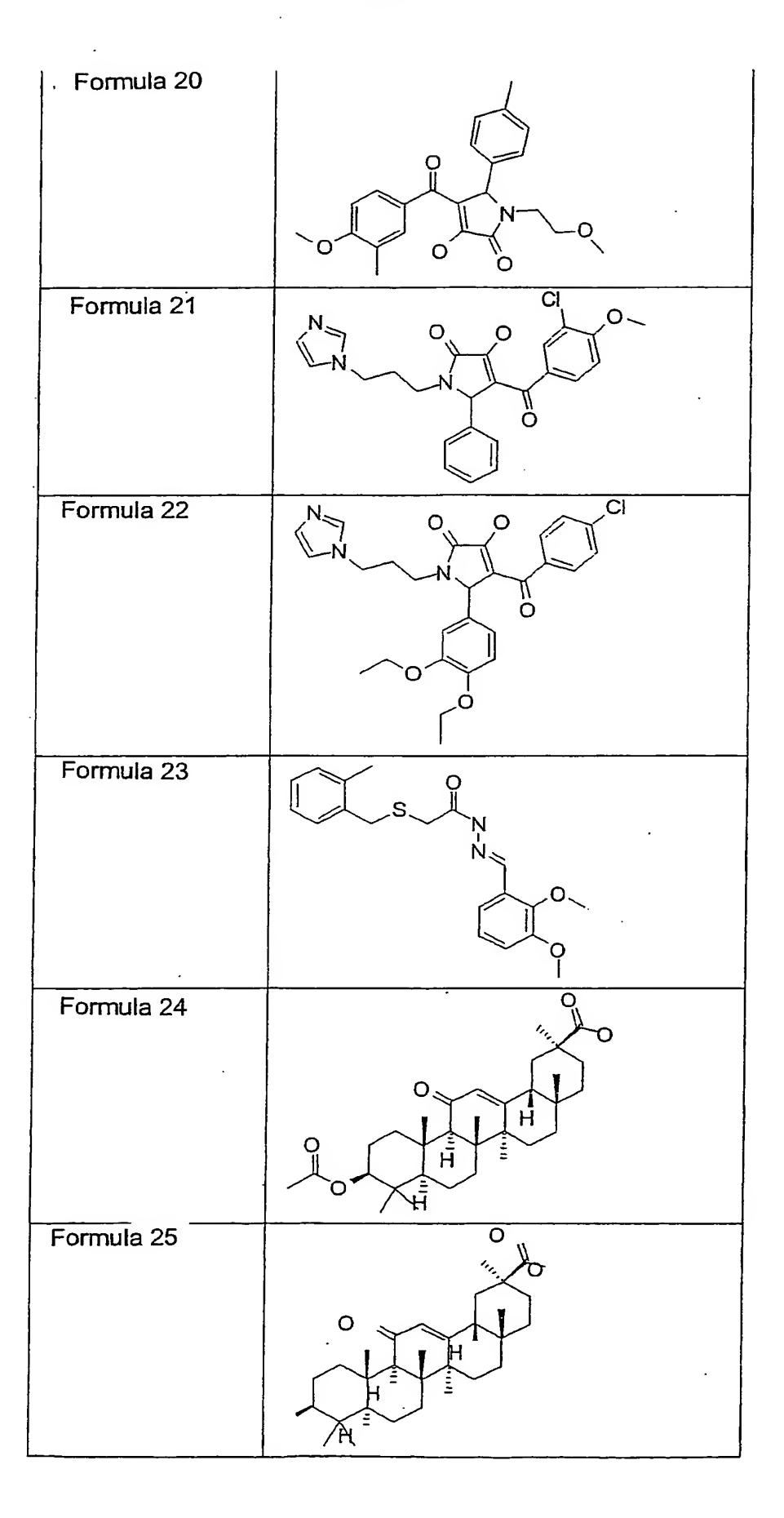
- 12. The use of any one of claims 1 to 11, wherein the pharmaceutical agent comprises at least one 11-β-HSD-type 1 and/or type 2 inhibitor in combination with at least one active ingredient being effective in the prevention and/or treatment of inflammation-induced and/or immunemediated loss of bone and/or cartilage.
- 13. The use according to any one of claims 1 to 12, wherein the pharmaceutical agent is administered in a dose of 5 to 100 mg/kg body weight per day.
- The use of any one of claims 1 to 13, wherein the pharmaceutical agent is administered orally, sublingually, intravenously, intramuscularly, intramedullarily, intrathecally, intraarterially, intraarticularly, intraocularly, intracerebrally, intracranially, intraventricularly, nasopharyngeally, transdermally, intratracheally, respiratorally, intradermally, subcutaneously, intraperitoneally, intranasally, enterally, topically, via rectal means, via infusion and/or via implant.
- 15. The use according to claim 14, wherein the pharmaceutical agent is administed orally.

16. A pharmaceutical composition comprising, as an active ingredient, an 11- β -HSD-type-1 and/or type 2 inhibitor or a salt thereof and a pharmaceutically acceptable carrier or diluent, wherein said 11- β -HSD-type 1 and/or type 2 inhibitor is selected from the group consisting of the following formulas 1 to 31:

Compound	Structure
Name	
Formula 1	
Formula 2	Br O O N N N N N N N N N N N N N N N N N
Formula 3	
Formula 4	
Formula 5	
Formula 6	

F	ormula 7	
F	ormula 8	N O N O O O O
F	ormula 9	CI CI CI
F	ormula 10	ONS ON-N SON
Fo	ormula 11	
F	ormula 12	
F	ormula 13	





Formula 26	
Formula 27	
Formula 28	
Formula 29	$ \begin{array}{c} N \\ N \\ O = S = O \end{array} $ $ \begin{array}{c} N \\ O \\ N - N \end{array} $
Formula 30	
Formula 31	Br CI

1

- 17. A pharmaceutical composition, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor has the structure of formula I as claimed in claim 7.
- 18. The pharmaceutical composition of claim 17, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor is selected from the group consisting of the formulas: 13, 14, 24 and 25 as claimed in claim 8.
- 19. A pharmaceutical composition, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor has the structure of formula II as claimed in claim 9.
- 20. The pharmaceutical composition according to claim 19, wherein the 11β-HSD-type 1 and/or type 2 inhibitor is formula 16 as claimed in claim 10.
- 21. A pharmaceutical composition, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor is formula 7 as claimed in claim 11.
- 22. The pharmaceutical composition of any one of claims 16 to 21 for the prevention and/or treatment of inflammation-induced and/or immune-mediated loss of bone and/or cartilage.
- 23. The pharmaceutical composition of any one of claims 16 to 22, for the prevention and/or treatment of osteoporosis, postmenopausal osteoporosis, Paget's disease, lytic bone metastases, arthritis, osteoarthritis, rheumatoid arthritis, juvenile chronic arthritis, chronic arthritis, adjuvant arthritis, infectious diseases, bone loss by cancer, bone loss by HIV, periodontitis, bone marrow inflammation, synovial inflammation, cartilage/bone erosion and/or proteoglycan damage.
 - 24. The pharmaceutical composition of any one of claims 16 to 23, further comprising at least one active ingredient being effective in the prevention and/or treatment of inflammation-induced and/or immunemediated loss of bone and/or cartilage.

WO 2005/027882 PCT/EP2004/010582

- 84 -

- 25. The pharmaceutical composition of any one of claims 16 to 24, for oral, sublingual, intravenous, intramuscular, intraarticular, intraarterial, intramedullary, intrathecal, intraventricular, intraocular, intracerebral, intracranial, respiratoral, intratracheal, nasopharhyngeal, transdermal, intradermal, subcutaneous, intraperitoneal, intranasal, enteral and/or topical administration and/or administration via rectal means, via infusion and/or via implant.
- 26. The pharmaceutical composition of any one of claims 16 to 25, being administered in a dose of 5 to 100 mg/kg body weight per day.
- 27. Pharmaceutical composition of any one of claims 16 to 26 for the inhibition of osteoclast activity.